REMARKS/ARGUMENTS

I. Status of the Claims

Claims 3, 4, 6, 8, 17-28, 34-38 are currently pending. Claims 3, 4, 6, 8, 17-18, 34, 36 and 38 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Maertens et al (Maertens et al. WO 96/13590, 9 May 1996). Claims 3, 4, 6, 8, 17-18, 34, 36 and 38 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Maertens et al (US 2002/0183508 Al, December 5, 2002). Claims 3, 4, 6, 8, 17-18, 34, 36 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Donnelly et al (WO 97/47358, 18 December 5, 1997). Claims 17, 18, 20-27 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Maertens et al (Maertens et al. WO 96/13590, 9 May 1996) or Maertens et al (Maertens et al. US 2002/0183508 Al, December 5, 2002) or Selby et al (J. *Gen. Virol.* **74**:1103-1113, 1993) or Donnelly et al (WO 97/47358, 18 December, 1997) in view of Tokushige et al *Hepatology* **24**:14-20, 1996) and Ferrari et al (*Hepatology* **19**:286-295).

II. Patentability under 35 U.S.C. § 102(b)

Claims 3, 4, 6, 8, 17-18, 34, 36 and 38 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Maertens et al (Maertens et al. WO 96/13590, 9 May 1996). Applicants traverse the rejection.

Applicants' claimed invention is novel in view of the Maertens PCT application. The Office alleges that the Maertens PCT application teaches a recombinant expression vector comprising a polynucleotide sequence expressing NS4, NS5, and a 5' UTR of hepatitis C virus. Applicants' claimed invention is directed to a recombinant nucleic acid molecule comprising a nucleotide sequence encoding a fusion protein of hepatitis C virus NS4 or NS5 protein or any combination thereof, wherein said nucleotide sequence is operably linked to regulatory elements, said regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and a 5' untranslated region (5'-UTR), said 5'-UTR comprising at least the 9 most 3' nucleotides of a 5' UTR of hepatitis C virus. Applicants' claimed invention is further directed to a method of inducing an immune response against hepatitis C virus utilizing a recombinant nucleic acid molecule encoding a fusion protein of hepatitis C virus NS3, NS4 or NS5 protein or any combination thereof. The Maertens PCT application

does not teach or suggest a recombinant nucleic acid molecule or a method of inducing an immune response against hepatitis C virus wherein the nucleic acid molecule encodes a fusion protein of hepatitis C virus NS3, NS4 or NS5 protein or any combination thereof. Therefore, claims 3, 4, 6, 8, 17-18, 34, 36 and 38 are novel in view of the Maertens PCT application.

Claims 3, 4, 6, 8, 17-18, 34, 36 and 38 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by the Donnelly et al. application (WO 97/47358, 18 December 1997). Applicants traverse the rejection.

The rejection of claims 3, 4, 6, 8, 17-18, 34, 36 and 38 under 35 U.S.C. § 102(b) in view of the Donnelly et al. application (WO 97/47358) is obviated because the Donelly et al. application was not "described in a printed publication more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b). The instant application (U.S. serial no. 09/600,493 claims priority under 35 U.S.C. § 371 to PCT/US99/01823, filed January 28, 1999, which claims benefit of U.S. provisional application 60/073,156, filed January 20, 1998. The priority date of the instant application, January 20, 1998, is within one year of the publication date of the Donelly et al. PCT application, December 18, 1997. A rejection under 35 U.S.C. § 102(b) in view of the Donnelly et al. application (WO 97/47358) cannot be maintained and is moot.

III. Patentability under 35 U.S.C. § 102(e)

Claims 3, 4, 6, 8, 17-18, 34, 36 and 38 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Maertens et al (US 2002/0183508 Al, December 5, 2002). Applicants traverse the rejection.

Applicants' claimed invention is novel in view of the Maertens U.S. application. The Office alleges that the Maertens U.S. application teaches a recombinant expression vector comprising a polynucleotide sequence expressing NS4, NS5, and a 5' UTR of hepatitis C virus. Applicants' claimed invention is directed to a recombinant nucleic acid molecule comprising a nucleotide sequence encoding a fusion protein of hepatitis C virus NS4 or NS5 protein or any combination thereof, wherein said nucleotide sequence is operably linked to regulatory elements, said regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and a 5' untranslated region (5'-UTR), said 5'-UTR comprising at

least the 9 most 3' nucleotides of a 5' UTR of hepatitis C virus. Applicants' claimed invention is further directed to a method of inducing an immune response against hepatitis C virus utilizing a recombinant nucleic acid molecule encoding a fusion protein of hepatitis C virus NS3, NS4 or NS5 protein or any combination thereof. The Maertens U.S. application does not teach or suggest a recombinant nucleic acid molecule or a method of inducing an immune response against hepatitis C virus wherein the nucleic acid molecule encodes a fusion protein of hepatitis C virus NS3, NS4 or NS5 protein or any combination thereof.. Therefore, claims 3, 4, 6, 8, 17-18, 34, 36 and 38 are novel in view of the Maertens U.S. application.

IV. Patentability under 35 U.S.C. § 103(a)

Claims 17, 18, 20-27 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Maertens et al (Maertens et al. WO 96/13590, 9 May 1996) or Maertens et al (Maertens et al. US 2002/0183508 Al, December 5, 2002) or Selby et al (J. *Gen.Virol.* **74**: 1103-1113, 1993) or Donnelly et al (WO 97/47358, 18 December, 1997) in view of Tokushige et al *Hepatology* **24**: 14-20, 1996) and Ferrari et al (*Hepatology* **19**:286-295). Applicants traverse the rejection.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation to modify the reference or to combine the reference teachings so as to arrive at the claimed invention and there must be a reasonable expectation of success for achieving the claimed invention as a whole. *See In re Vaeck*, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991). For the reasons discussed below, a proper *prima facie* case of obviousness has not been set forth, because no suggestion or motivation to modify or combine the references is given so as to arrive at the claimed invention.

Independent claim 17 is now directed to a method of inducing an immune response against hepatitis C virus in a human uninfected by hepatitis C virus comprising administering to said human a recombinant nucleic acid molecule comprising a nucleotide sequence encoding a fusion protein of hepatitis C virus nonstructural proteins NS3, NS4, or NS5, or any combination thereof, in an amount effective to induce an immune response against hepatitis C virus. The cited references fail to teach or suggest such method of inducing an immune response.

As stated above, a rejection under 35 U.S.C. § 103(a) in view of the Donnelly et al. application (WO 97/47358) cannot be maintained since the publication date of the Donelly et al. reference is within one year of the priority date of the instant application.

The Office Action provides no suggestion or motivation to modify the reference or to combine the reference teachings so as to arrive at the claimed invention with any expectation of success. The Office Action cites the Maertens et al. PCT application, the Maertens et al. U.S. application or the Selby et al. reference as teaching a recombinant expression vector that express NS4, NS5, and the 5'UTR of hepatitis C virus. The Office Action cites the Selby et al. reference as teaching a recombinant expression vector that expresses NS4-NS5 fusion protein. The Office Action cites the Tokushige et al. reference as teaching a method of producing immune response to hepatitis C core protein and further cites the Ferrari et al reference as teaching a T cell response to core protein is greater than a T cell response to NS5 protein.

The claimed invention provides a method of inducing an immune response against hepatitis C virus comprising administering to the human a recombinant nucleic acid molecule comprising a nucleotide sequence encoding a fusion protein of hepatitis C virus nonstructural proteins NS3, NS4, or NS5, or any combination thereof, in an amount effective to induce an immune response against hepatitis C virus. The combination of references do not teach applicants' claimed invention. The references teach vectors that express a polyprotein, for example, pEMCV-C-E1-E2-NS2-NS3-NS4-NS5, or pEMCV- NS2-NS3-NS4-NS5, as in the Selby et al. reference. The references further teach immune response to individual HCV core, structural, or non-structural proteins, as in the Ferrari et al. or Tokushige et al. references. The cited references provide a nucleic acid molecule encoding an HCV polyprotein and an immune response to nucleic acids encoding individual HCV proteins. By contrast, the claimed invention provides a nucleic acid encoding a fusion protein of HCV proteins NS3, NS4, or NS5, or any combination thereof, that induces an immune response to the fusion protein. The cited references do not provide a reasonable expectation of success in achieving a method of inducing an immune response by administering a nucleic acid encoding a fusion protein of HCV proteins NS3, NS4, or NS5, or any combination thereof. The claimed invention as a whole advantageously allows the use of nucleic acid molecules encoding a fusion protein of HCV NS3, NS4, or NS5, or any combination thereof, to induce

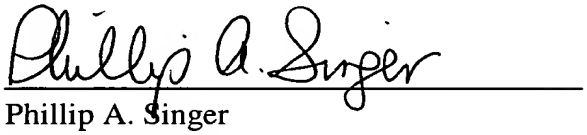
encoding a fusion protein of HCV proteins NS3, NS4, or NS5, or any combination thereof. The claimed invention as a whole advantageously allows the use of nucleic acid molecules encoding a fusion protein of HCV NS3, NS4, or NS5, or any combination thereof, to induce an immune response in a human. Since the claims patentably define over the prior art, Applicants respectfully request that the rejection of claims 17, 18, 20-27 under 35 U.S.C. § 103(a) be withdrawn.

V. Conclusion

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-332-1380.

Date: January 21, 2004



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